(TENS) for the treatment of pain is contraindicated in patients with pacemakers. To test if TENS is safe in patients with *newer* pacemakers, we studied 24 male patients (ages 74.5 ± 5.2 years) with pacemakers implanted after 1/1/90. TENS (frequency 85 Hz, pulse width 100 us, amplitude 46 ± 8 mA) was applied on the shoulders, upper, mid, and lower back, precordium and the site of pacemaker generator. Interelectrode distance for TENS was 5 cm. Partial inhibition/interference during TENS application on the chest close to the pacemaker generator was noted in 1/18 patients, when the pacemaker was programmed in bipolar mode, and in 6/13 patients, when the pacemaker was in unipolar mode. Ten of the 24 patients with chronic pain went on to use TENS in various areas of the body except the chest for 308 ± 68 days. Of these ten patients, seven had bipolar and three had unipolar pacemakers. In six of these ten patients, the pacemaker was in VVI mode and four in DDD mode. Holter monitoring performed every 3 months in these patients revealed no inhibition/interference of the pacemakers.

Conclusion: After thorough evaluation and programming, long-term use of TENS in patients with newer pacemakers and chronic pain is safe. These patients should be told that TENS can be applied to any part of the body except the chest.

1089-133 The Equivalent Circuit of Pacing in the Limit as Surface Area goes to Zero: A Complex Impedance Plane Analysis

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Smaller surface area electrodes are being deployed clinically to increase resistance and reduce power output. However the equivalent circuit of cardiac pacing has never been studied in living heart at smaller electrode surface areas. It is not known whether qualitative differences exist at smaller surface area. For sensing the behavior is exquisitely dependent on the equivalent circuit, particularly configuration of capacitances and resistances. *Methods* The pacing equivalent circuit was determined for Pt wire electrodes implanted acutely in open chest rats, both (A) for a series of electrodes of reduced exposed surface (0.9–12 mm^2, n = 16) and (B) for glass encased Pt electrodes of same diameter but with only the end exposed (0.049 mm^2, n = 8). Thévenin capacitance & resistance were measured for series (A) and limit (B), via AC impedance spectroscopy in a potentiostatic 3-electrode arrangement, with a 7–13 mV sine wave at 50 Hz to 1.24 MHz, signal averaging and single op amp *i*-V converter with waveform sampling at ≤ 100 MS/s (MHz). Complex impedance plane analysis was performed. *Results:* Capacitance versus surface area relation was determined for series A and found to be a straight line, implying that the series element of the conducting interface is precisely the electrode surface area with *no* modifying geometrical factor. Capacitance was an extensive linear function of surface area with slope 53 ± 11 nF/mm^2. Impedance plane analysis, however disclosed *discontinuous* behavior with unanticipated emergence of Cole-Cole semicircular at lowest surface areas, universally seen in (B).

Conclusion: The discontinuous behavior implies *a different equivalent circuit* for smaller electrodes with a new finite-conductance *parallel* circuit element present even at higher frequencies at the capacitative interface. A different equivalent circuit applies at smallest surface area. This is relevant for cardiac pacing, since the depolarizing current pathway with these electrodes may well be of this order of magnitude. This is the first reported measurement of interfacial measurements in the limiting case of low surface area electrode in living perfused heart.

1090 Basic Electrophysiology: Ion Channels

Wednesday, March 19, 1997, 3:00 p.m.–5:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 3:00 p.m.–4:00 p.m.

1090-83 Effects on Repolarization of the Chromanol 293B, a Highly Selective Blocker of the Slow Component of the Delayed Rectifier K^+ Current (I_{Ks}) in Human and Guinea Pig Ventricle

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There has been controversy about the physiologic role of I_{Ks} and the potential of I_{Ks} blockade as an antiarrhythmic mechanism, largely because of the absence of highly-selective I_{Ks} blocking drugs. Chromanols are potent, selective blockers of minK expressed in oocytes. We studied the electrophysiologic properties of the derivate 293B in human (H) and guinea pig (GP) ventricular myocytes with the whole cell patch-clamp technique. Using 3-s depolarizing pulses, 293B blocked GP I_K step current at +50 mV in a concentration-dependent manner with an IC_{50} of 1.02 μM, while I_K at −10 mV (largely the rapid component I_{Kr}) was unaffected by concentrations up to 50 μM (98.6 ± 8.4% of control, n = 7). For long test pulses (3s) to +50 mV, 50 μM 293B blocked I_K tail currents (on repolarization to −40 mV) by 92.3 ± 6.6%, whereas for short pulses (225 ms) the corresponding values were 19.5 ± 5.9%. Half-activation voltages for the 293B sensitive (SEN) and resistant (RES) I_K averaged 30.9 ± 0.4 mV and −17.1 ± 1.0 mV (n = 7), and the form of the I–V relations for SEN and RES were typical of I_{Ks} and I_{Kr} respectively. RES had a similar current density to dofetilide-sensitive I_{Kr}, (eg at 0 mV RES was 0.30 ± 0.06 pA/pF and I_{Kr} 0.31 ± 0.04 pA/pF), SEN and dofetilide resistant I_{Ks} densities were also similar (ie, at +50 mV: 2.6 ± 0.7 and 2.5 ± 0.4 pA/pF). I_{K1}, I_{Ca} and I_{Na} in H and GP ventricle were not affected by 293B. I_{to} in H cells was inhibited by concentrations 20-fold greater than those inhibiting I_{Ks} (IC_{50} = 24.0 μM). 293B (1 μM) significantly prolonged action potential duration to 90% repolarization (APD_{90}) in a frequency-independent manner (at 4 Hz from 91 ± 4 ms in controls to 117 ± 8 ms [29%, $p < 0.05$], at 1 Hz from 124 ± 5 to 167 ± 19 ms [33%]). *Conclusion:* 293B is a highly selective blocker of I_{Ks}, and therefore a very useful tool for assessing the role of I_{Ks} and the potential of I_{Ks} blockers to treat arrhythmias.

1090-84 Evidence for Ca^{2+}-Activated Transient Outward Chloride Currents in Ventricular Cells From Human Hearts

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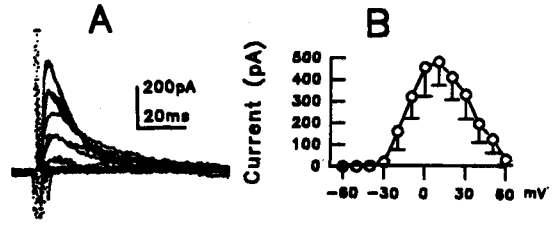
Ca^{2+}-activated transient outward chloride currents ($I_{Cl,Ca}$ or I_{to2}) have been described in rabbit and dog cardiac myocytes. However, $I_{Cl,Ca}$ appears absent in human atrium and has not been demonstrated in human ventricle. The present study was designed to detect $I_{Cl,Ca}$ in ventricular myocytes using whole cell voltage-clamp at 36ºC. Low pipette EGTA (0.05 mM) was used in all cells. Ventricular myocytes from 3 explanted human hearts were depolarized with 200-ms voltage steps between −60 and +60 mV from a holding potential of −80 mV. Membrane currents were recorded before and after exposure to 5 μM ryanodine. Ryanodine-sensitive transient outward currents were observed after current subtraction in 9 of 11 cells (Fig A). The I–V relation of the current was bell-shaped, and peaked at +10 mV (Fig B). Similar 4-Ap resistant currents were detected by $[Cl^-]_o$ replacement by methanesulfonate in 4 other cells. The current clearly is 4AP-resistant.



These results indicate that ryanodine-sensitive Cl currents typical of $I_{Cl,Ca}$ are present in the human ventricle, where they may play an important and previously unrecognized role in action potential repolarization.

1090-85 Dynamics of Ca^{2+} Transients in Initiation of Early Afterdepolarizations and Triggered Ventricular Tachycardia: Effects of Ryanodine and Verapamil in Isolated Rabbit Hearts

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To assess role of cytosolic free Ca^{2+} in initiation of early afterdepolarizations (EAD) and triggered ventricular tachycardia (VT), we studied effects of ryanodine (R) and verapamil (V) in Langendorff-perfused rabbit hearts. After creation of atrioventricular block, clofilium (C) (5.5 μM) was infused to induce EAD and triggered VT during which fluorescent Ca^{2+} indicator–fura red (10 μM) was loaded and monophasic action potentials (MAP) were recorded. In group 1 control (n = 9), C significantly prolonged MAP duration (MAP_{50}: 202 ± 43 → 272 ± 64 ms; MAP_{90}: 298 ± 39 → 460 ± 88 ms, $p < 0.05$) and induced EAD and/or triggered VT in 9/9 (100%) hearts. C increased both end-diastolic and peak-systolic Ca^{2+} transients, but increments did not reach statistical significance. In group 2, pretreated with R (1 μM) (n = 6), R did not prevent C-induced MAP prolongation, but suppressed inducibility of EAD